

REMARKS

The foregoing amendment amends independent claims 1, 9, 20, 42, 64 and 66 and dependent claim 56. Pending in the application are claims 1-69, of which claims 1, 9, 20, 22, 29, 42, 64, 65, 66 and 67 are independent. Claims 2-8, 22-41, 49-54, 59, 60 and 67-69 are withdrawn from consideration. The following comments address all stated grounds for rejection and place the presently pending claims, as identified above, in condition for allowance.

Independent claims 1, 9, 42, 64 and 66 are amended to specify that each fluid interface port has a dead volume that is less than about 1 picoliter. Support for the amendment can be found throughout the application as filed, at least for example, on page 22, lines 15-18.

Independent claim 20 is amended to specify that the microchannel has a diameter of between about 25 μm and about 100 μm , that the first filling aperture has a diameter that is substantially equal to the diameter of the microchannel and that the second filling aperture has a third diameter that is substantially equal to the diameter of the microchannel. Support for the amendment can be found throughout the application as filed, at least for example, on page 16, lines 6-9, and lines 30-33, and on page 22, lines 4-7.

Claim 56 is amended to change the word "fluid" to ---second liquid---, which has antecedent basis in lines 1 and 3 of claim 42, from which claim 56 depends. *No new matter is added.*

Amendment and/or cancellation of the claims is not to be construed as an acquiescence to any of the objections/rejections set forth in the instant Office Action, and was done solely to expedite prosecution of the application. Applicant reserves the right to pursue the claims as originally filed, or similar claims, in this or one or more subsequent patent applications.

Response to Restriction Requirement

Applicants confirm the election of Group I, species A, with traverse, in response to the Restriction Requirement.

Objections to the Drawings

Regarding the objection to the drawings for failing to comply with 37 CFR 1.84(p)(5), Applicants have amended the drawings and specification to address the Examiner's concerns. Specifically, Applicants have amended the paragraph describing Figure 11c, beginning on page 28, line 29 and extending to page 29, lines 8 to change the phrase "targeting electrode 61" to --targeting electrode 60--, which is consistent with Figure 11c. Applicants also amend Figure 11A to include reference sign 57, Figure 11B to include reference signs 15 and 17 and Figure 18 to include reference sign 181. In addition, Applicants amend Figure 9F to move the reference arrow for virtual wall 15 to point to the lower meniscus forming the virtual wall, rather than the encapsulant 66.

Corrected drawing sheets with the corrections marked in red are attached to this Response. Replacement sheets incorporating the corrections are also attached.

Claim Objections

Regarding the objection to claim 56 is objected for failing to provide antecedent basis for the term "fluid", Applicants have amended claim 56 to change the word "fluid" to ---second liquid---, which has antecedent basis in lines 1 and 3 of claim 42, from which claim 56 depends, and request that the objection be reconsidered and withdrawn.

Claim Rejections Under 35 USC § 102

Claims 1, 42, 48, 56, 58, 64 and 65 are rejected under 35 U.S.C. §102(b) as being anticipated by Howitz et al. The Examiner rejects claims 9-12, 14, 15, 20 and 21 under 35 U.S.C. §102(b) as being anticipated by Columbus (U.S. Patent Number 4,302,313) The Examiner rejects claims 9, 10, 14, 15, 42 and 55 under 35 U.S.C. §102(b) as being anticipated by Columbus (U.S. Patent Number 4,426,451). Applicants respectfully traverse the rejection for the following reasons.

The Howitz reference discloses a fluid microdiode for incorporating a dosed fluid into a target fluid contained in a closed system. According to the Examiner, because the Howitz reference discloses jetting a dosed fluid on a coupling surface comprising an array of

microcapillaries forming micromenisci so as to introduce the dosed fluid to a target fluid in a flow channel that forms the micromenisci, claims 1, 42, 48, 56, 58, 64 and 65 are anticipated.

However, the microcapillaries of Howitz do not have a dead volume that is less than about one picoliter, as recited in independent claims 1, 42 and 64. As set forth in the specification, “dead volume” refers to the volume of liquid retained in a fluid interface port (i.e. the volume of liquid the fluid interface port holds that is not flushed through the fluid interface port by the flow field of the first liquid through the microchannel). Each microcapillary in Howitz has a dead volume that is significantly greater than one picoliter, due to the relatively large height of the microcapillaries. In contrast, the claimed fluid interface ports have a significantly smaller dead space, in part due to the smaller thickness of the side walls of the channel in comparison to the FMD chip of Howitz.

The relatively small dead volume provided by the virtual wall in the claimed methods results in a direct fluid interface allowing direct injection of a precise volume of sample into the interior of a microchannel from the exterior of the microchannel. The ability to directly inject sample into the microchannel due to the low dead volume of the fluid interface port provides improved control over the amount of sample that is injected into the microchannel, allows efficient use of sample, and significantly reduces waste of the sample. Furthermore, the direct injection provided by the very small dead volume reduces or prevents cross-contamination between different samples and allows a third liquid to be directly injected into the system immediately after a second liquid without requiring flushing of the fluid interface port. Conversely, the larger dead volume in Howitz may lead to dispersion of the sample, a time delay between the time of injection and the time when the sample enters the microchannel, injection inefficiency, potential cross-contamination between different samples and difficulty controlling the amount of sample that actually reaches the microchannel. These problems are avoided or reduced by the use of the fluid interface port forming a virtual wall having a dead volume of less than about one picoliter according to the illustrative embodiment.

Furthermore, the menisci 6 formed in the microcapillaries of the device of Howitz also do *not* comprise “virtual walls”, as recited in independent claims 1, 42, 64 and 65. A virtual wall refers to a particular type of meniscus formed in a fluid interface port, but is not *any* and every

type of meniscus (i.e., all menisci are not virtual walls). The term “virtual wall” is used to denote that the meniscus formed by a fluid in the fluid interface port essentially replaces the removed portion of the side wall that forms the port. The word ‘virtual’ in the present claims refers to the effect that the overall liquid flow through the separation channel of the electrophoretic system is not influenced by the virtual wall, i.e. the flow of liquid in the micro-plate having a virtual wall is substantially identical to the flow of liquid through an identical micro-plate in which no virtual wall is formed.

There is no teaching or suggestion in Howitz that the micromenisci 6 essentially replace the side wall of the flow channel 7, or that the presence of the microcapillaries does not influence the flow of fluid through the flow channel.

Regarding the rejection of claims 9-12, 14, 15, 20 and 21 under 35 U.S.C. 102(b) as being anticipated by Columbus (US 4,302,313), Applicants submit that pending claims 9-12, 14, 15, 20 and 21 distinguish patentably over the cited Columbus ‘313 reference because the Columbus ‘313 reference does not disclose a step of directing a droplet of liquid through a fluid interface port having a dead volume of less than one picoliter, as recited in independent claim 9, or a first and second filling aperture having a diameter between about 25 μm and about 100 μm , and substantially equal to the diameter of a corresponding microchannel, as recited in independent claim 20.

The Columbus ‘313 reference is directed to a device for analyzing fluid, including a flow control bridge 36 for providing means for directing liquid flow from drops to ion-selective electrodes 14, 14’. The drops are introduced through liquid ingress apertures 27 to a zone 41. The apertures have a relatively long length and size, resulting in a dead volume that is significantly larger than one picoliter. For example, on page 9, lines 6-8, the Columbus reference indicates that it is preferable for a liquid ingress aperture 27b in a flow control bridge to have a diameter of about 0.25 centimeters, which would result in a relatively large dead volume.

In addition, the 0.25 centimeter diameter of the liquid ingress apertures of the Columbus '313 reference is significantly larger than the range of between about 25 μm and about 100 μm specified in claim 20. Moreover, the Columbus '313 reference lacks a teaching or suggestion of a plurality of filling apertures having diameters substantially equal to the diameter of an associated microchannel. Therefore the Columbus '313 reference fails to anticipate claims 9-12, 14, 15, 20 and 21.

Regarding the rejection of claims 9, 10, 14, 15, 42 and 55 under 35 U.S.C. 102(b) as being anticipated by Columbus (US 4, 426,451), Applicants submit that pending claims 9, 10, 14, 15, 42 and 55 distinguish patentably over the cited Columbus '451 reference because the Columbus '451 reference does not disclose a step of directing a droplet of liquid through a fluid interface port having a dead volume of less than one picoliter, as recited in independent claims 9 and 42, or through a fluid interface port forming a virtual wall, as recited in independent claim 42.

The Columbus '451 reference is directed to multi-zone reaction vessel and a method for controlling flow from one zone to another. The reaction vessel 20 of Columbus '451 includes a liquid inlet aperture 46 for permitting the introduction of liquid into zone 22 of the reaction vessel 20. As specifically set forth in column 5, lines 29-34, the liquid inlet aperture 46 has a diameter of between about 1.0 mm and about 5.0 mm, which would result in a dead volume many times larger than one picoliter, and is incapable of forming a virtual wall. Therefore, the Columbus '451 reference fails to anticipate claims 9, 10, 14, 15, 42 and 55.

Claim Rejections Under 35 USC § 103

Applicants also traverse rejection of claims 13, 16-19, 42-47, 57, 61-63 and 66 under 35 U.S.C. §103(a) as being obvious in view of various combinations of the cited references. The cited references, alone or in combination, fail to teach or suggest a step of directing a droplet through a fluid interface port having a dead volume of less than about one picoliter, as recited in independent claims 1, 9, 22, 29, 42, 64, 65, 66 and 67, or a fluid interface port having a diameter that is substantially equal to a diameter of an associated microchannel and between about 25 μm

and about 100 μm , as recited in independent claim 20. The cited references also fail to teach or suggest directing a droplet through a *virtual wall* of a fluid interface port, as recited in independent claims 1, 42, 64, 65 and 66. Therefore, dependent claims 13, 16-19, 43-47, 57 and 61-63 are also patentable. Furthermore, regarding the rejection of independent claim 66 as being unpatentable over the Howitz reference, Applicants submit that it would not be obvious in view of Howitz to have a fluid interface port having zero dead volume, or a dead volume that is less than one nanoliter or less than a picoliter. The Howitz reference requires that the microcapillaries have a relatively large dead volume, which teaches away from having the small dead volume claimed in the present invention.

Furthermore, the Examiner has not pointed to an object reason for combining the cited reference in rendering the conclusion that claims 13, 16-19, 42-47, 57, 61-63 and 66 are obvious. Therefore, the Examiner fails to make a proper *prima facie* case of obviousness.

For at least these reasons, Applicants respectfully submit that all pending examined claims are patentable, and request that the objections and rejections be reconsidered and withdrawn.

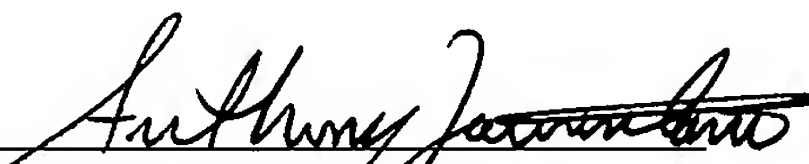
CONCLUSION

In view of the above amendment, applicants believe the pending application is in condition for allowance.

Applicants believe no fee is due with this statement. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. TGZ-001B from which the undersigned is authorized to draw.

Dated: January 27, 2005

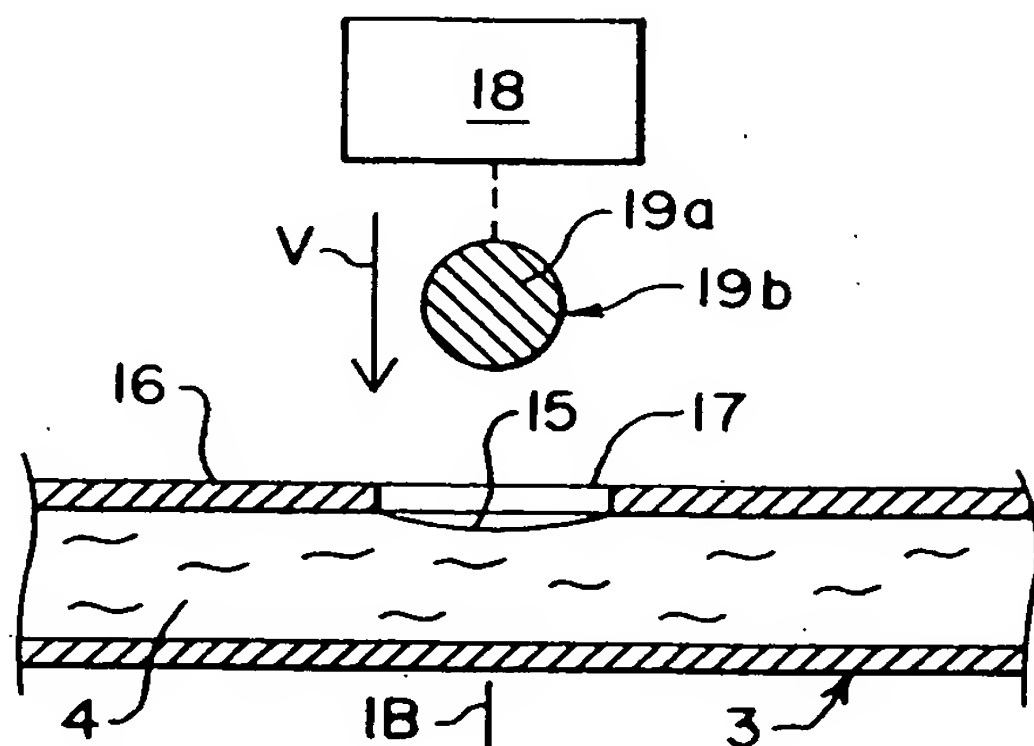
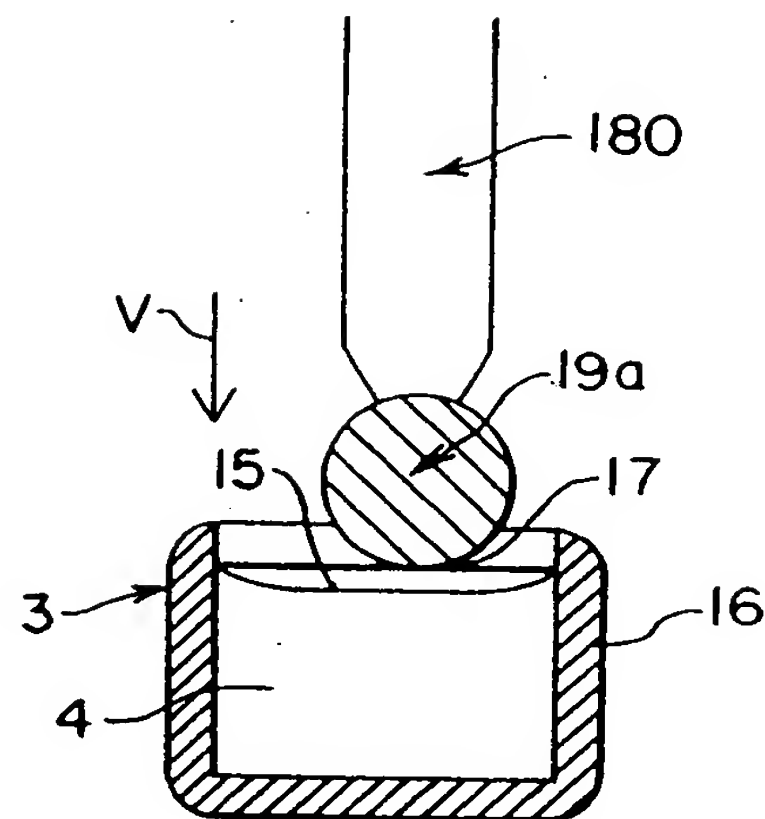
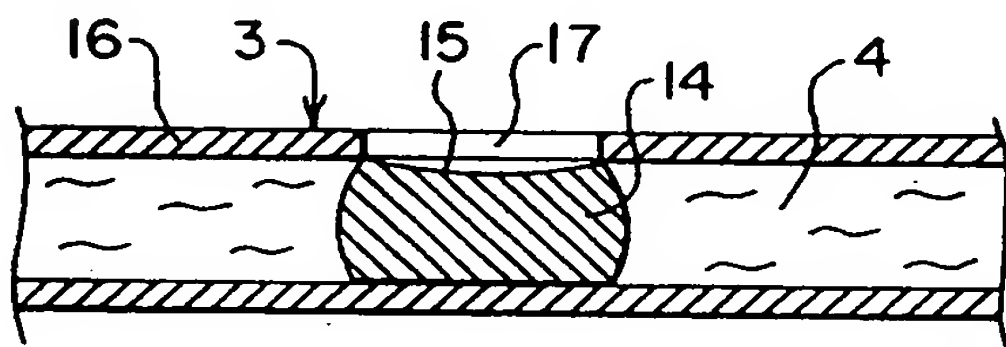
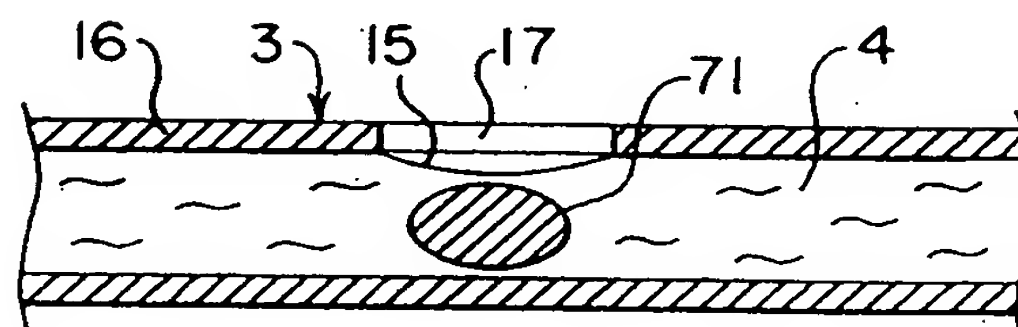
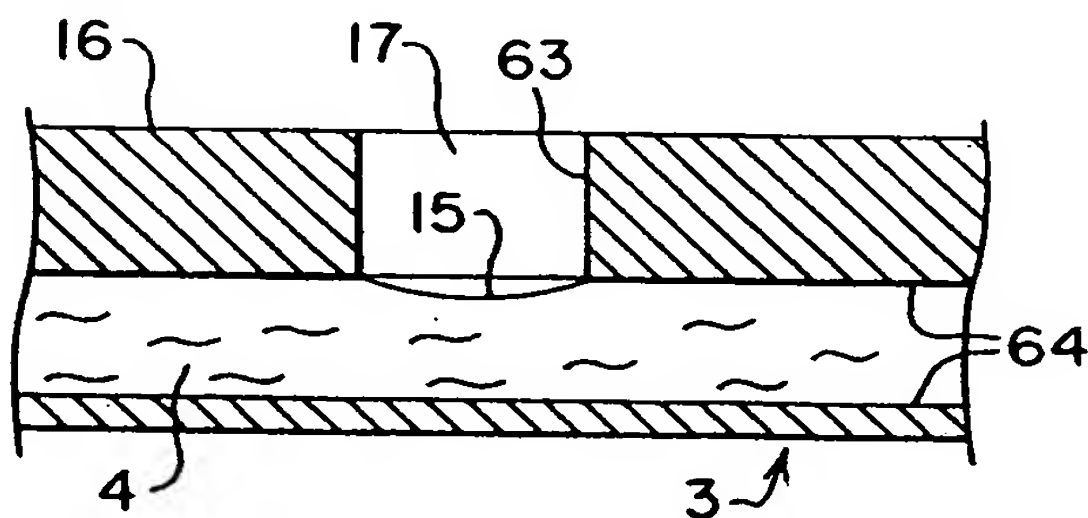
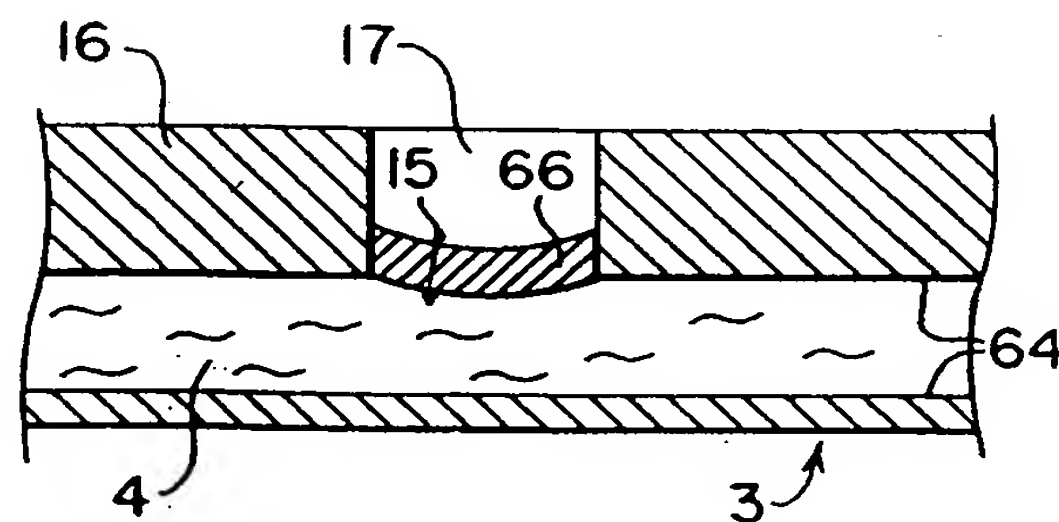
Respectfully submitted,

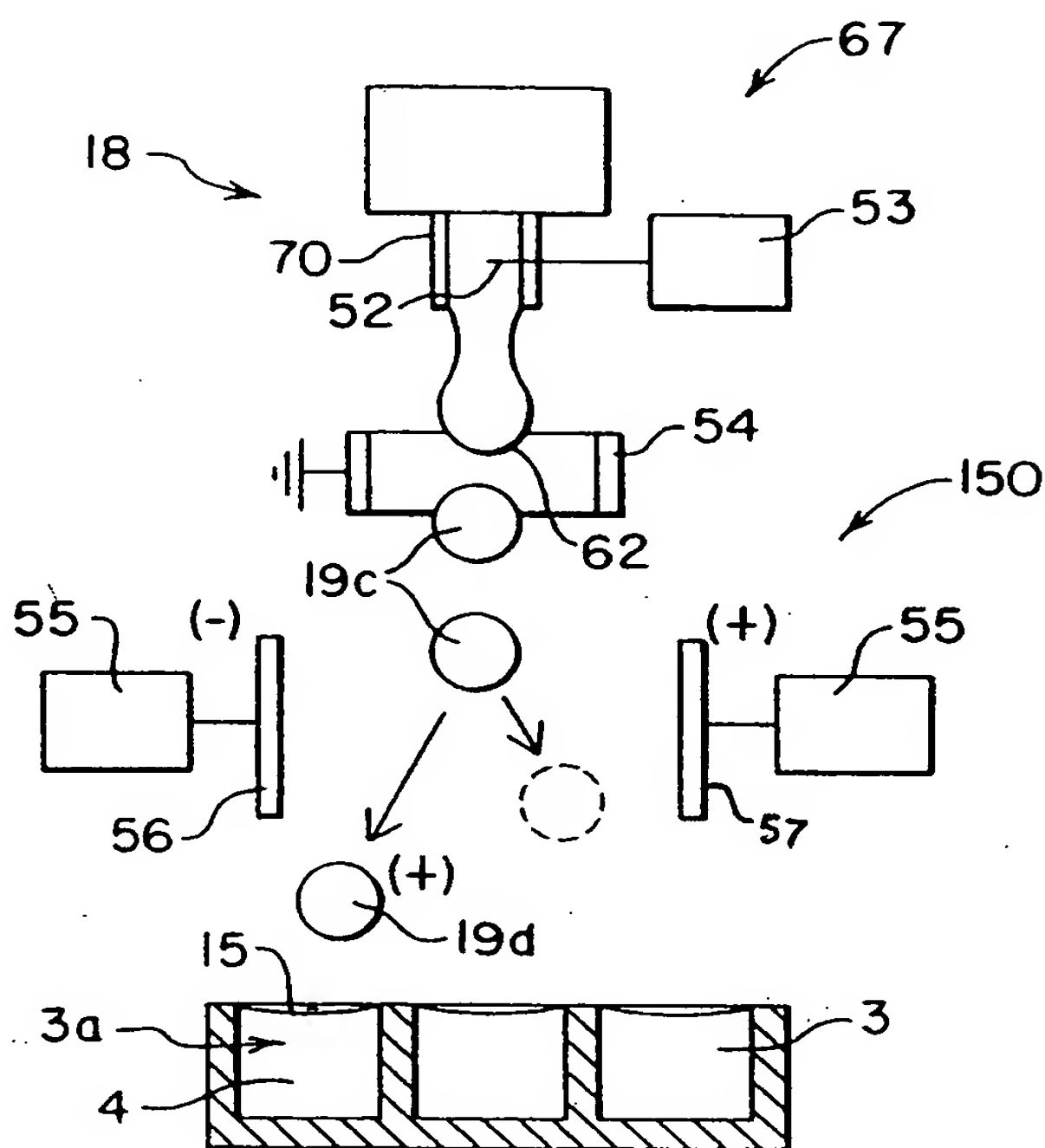
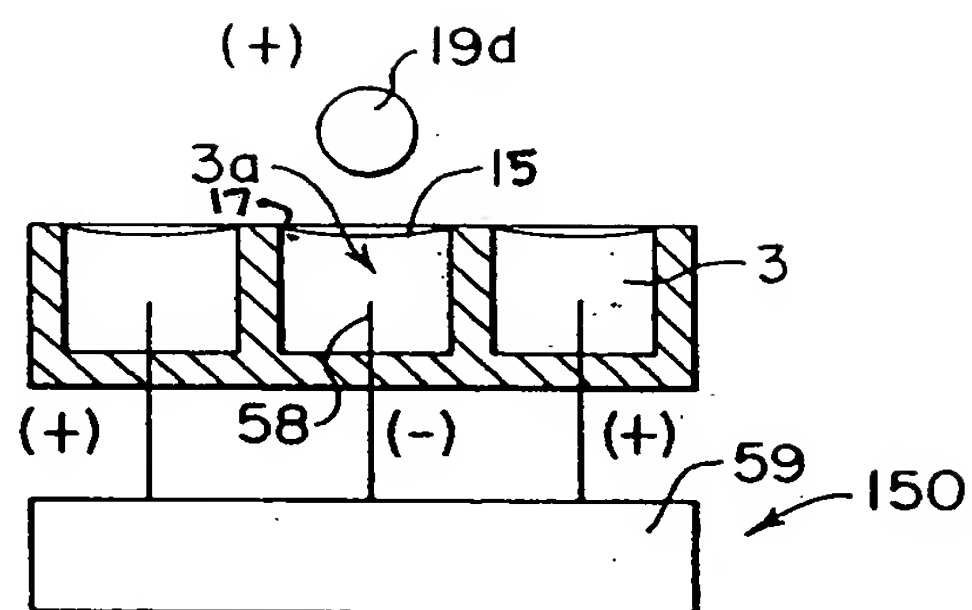
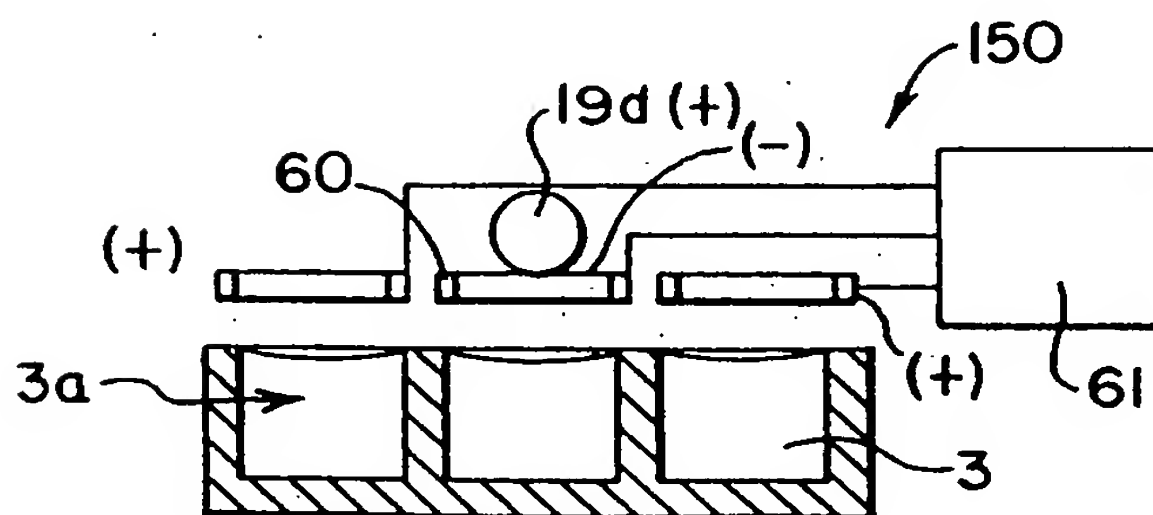
By 
Anthony A. Laurentano
Registration No. 38,220
LAHIVE & COCKFIELD, LLP
28 State Street
Boston, Massachusetts 02109
(617) 227-7400
(617) 742-4214 (Fax)
Attorney For Applicants

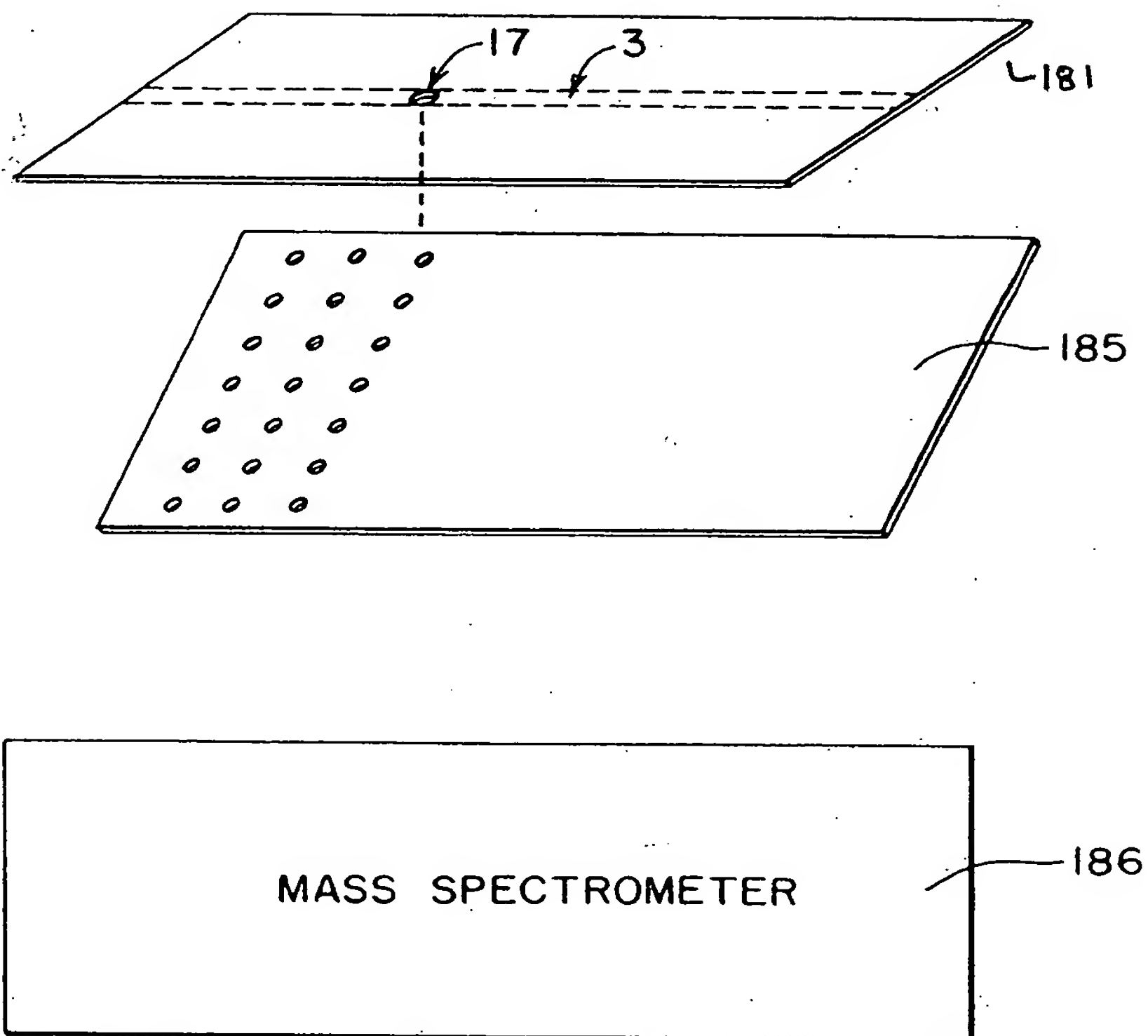
AMENDMENTS TO THE DRAWINGS

The attached three sheets of drawings include changes to Figures 9F, 11A, 11B and 18. These sheets, which include Figures 9A-9F, 11A-11C and Figure 18, respectively, replace the original sheets including Figures 9A-9F, 11A-11C and Figure 18.

Attachment: Three Replacement Sheets
Annotated Sheets Showing Changes in Red

**FIG. 9A****FIG. 9B****FIG. 9C****FIG. 9D****FIG. 9E****FIG. 9F**

**FIG. 11A****FIG. 11B****FIG. 11C**

***FIG. 18***